



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Ramnarayan *et al.*

Serial No.: 09/704,362

Confirmation No.: 4748

Filed: November 1, 2000

For: *USE OF COMPUTATIONALLY DERIVED
PROTEIN STRUCTURES OF GENETIC
POLYMORPHISMS IN
PHARMACOGENOMICS FOR DRUG
DESIGN AND CLINICAL APPLICATIONS*

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MARKED-UP CLAIMS (37 CFR §1.121)

IN THE CLAIMS:

Please amend claim 23 as follows:

23. (Amended) A computer-based method for predicting clinical responses in patients based on genetic polymorphisms, comprising:

obtaining one or more amino acid sequences for a target protein that is the product of a gene exhibiting genetic polymorphisms;

generating 3-D protein structural variant models from the sequences;

building a relational database of protein structural variants [derived] based on genetic polymorphisms and observed clinical data associated with particular polymorphisms exhibited in the patients, wherein the database comprises:

3-D molecular coordinates for [the] structural variant-drug complex models;

[a molecular graphics interface for 3-D molecular structure visualization;

functionality for protein sequence and structural analysis; database searching tools;] and

observed clinical data associated with the genetic polymorphisms;

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obtaining a target protein structural variant [based on the same]encoded by a gene [associated with a polymorphism]exhibiting genetic polymorphism in a patient;

generating a 3-D protein model based on the [subject's]patient's gene sequence;

[screening/comparing]screening or comparing the 3-D model derived from the [subject]patient to the structures contained in the database by:

identifying structures in the database that are similar to the model derived from the [subject]patient; and

predicting a clinical outcome for the patient based on the clinical data associated with the identified structures.